REMARKS

In the present communication, no claims have been amended; no claims have been canceled; and no claims have been added. Claims 2, 19 and 45-48 remain pending in this application.

Rejections under 35 U.S.C. §35 U.S.C. §103

Applicants respectfully traverse the rejection of claims 2, 19 and 45-48 under 35 U.S.C. §103 as allegedly obvious over Rothstein et al. (WO 0130968; hereinafter "Rothstein"), further in view of Wahle et al. (*J Cell Biol,* 135(6):1876-1877 (1996); hereinafter "Wahle").

The U.S. Supreme Court decision in the *KSR International v. Teleflex Inc.* (82 USPQ2d 1385), modified the standard for establishing a *prima facie* case of obviousness. Under the *KSR* rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

The *2010 KSR Guidelines Update* provides additional guidance in view of decisions by the United States Court of Appeals for the Federal Circuit (Federal Circuit) since *KSR*. However, familiar lines of argument still apply, including teaching away from the claimed invention by the prior art, lack of a reasonable expectation of success, and unexpected results. Indeed, such arguments may have even taken on added importance in view of the recognition in *KSR* of a variety of possible rationales. Federal Register, Vol. 75, No. 169, September 1, 2010, page 53645. Applicants respectfully submit that the Office has not met the burden of establishing a *prima facie* case of obviousness for the reasons discussed below.

The Office cites Rothstein as allegedly disclosing every element of the claimed method with the following exception. The Office acknowledges that Rothstein fails to disclose "detecting the level of glycosylation of a GTRAP3-18 target molecule…wherein the GTRAP3-

18 target molecule is glutamate transporter GLAST/EAAT1" as required by (b) of claim 2. To remedy the deficiency of Rothstein, the Office cites Wahle as allegedly disclosing methods for detecting the glycosylation state of the GLAST1 transporter.

Applicants point out that the claims are drawn to a method for identifying a compound which modulates cellular glycosylation, comprising: a) contacting a cell which expresses GTRAP3-18 with a test compound; and b) identifying the test compound as a modulator of cellular glycosylation by assaying the ability of the test compound to modulate the expression of a GTRAP3-18 nucleic acid molecule or polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, or the activity of a GTRAP3-18 polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, thereby identifying a compound which modulates cellular glycosylation, wherein the GTRAP3-18 target molecule is glutamate transporter GLAST/EAAT1.

The present invention is based on the seminal discovery that GTRAP3-18 acts as a general regulator of cellular glycosylation as opposed to modulating, for example, only glutamate transporters. The specification defines the invention as follows:

> The present invention is based, at least in part, on the discovery that the glutamate transporter regulatory protein GTRAP3-18 acts as a general regulator of cellular glycosylation, including glycosylation of neurotransmitter transporters and receptors, including glutamate transporters, dopamine transporters, GABA transporters, and amino acid transporters (ASCTs). Page 3, lines 19-23 of WO2004/065932.

The Office Action presents no *prima facie* case of obviousness since the cited references alone, or in combination, fail to teach each and every element of the claimed invention. In contrast to the present invention, Applicants assert that Rothstein discloses a protein-protein interaction between GTRAP3-18 and glutamate transporter proteins. The various methods disclosed in Rothstein are based on the disruption of the protein-protein interaction, for example, by inhibition of the interaction between GTRAP3-18 and a glutamate transporter protein. Rothstein, however, does not disclose the function of GTRAP3-18 as a general regulator of cellular

glycosylation. As such, Rothstein fails to disclose the ability of GTRAP3-18 to regulate glycosylation of a number of neurotransmitter transporters and receptors including glutamate transporters, dopamine transporters, GABA transporters, and amino acid transporters. Accordingly, Applicants assert that Rothstein does not disclose the method of the instant invention for identifying compounds that are capable of generally modulating cellular glycosylation. As such, Rothstein fails to disclose each and every element of the claimed invention.

Further, Wahle fails to remedy the deficiencies of Rothstein as it too fails to disclose the presently claimed method. As acknowledged by the Office, Wahle generally pertains to detecting the glycosylation state of the GLAST1 transporter. However, like Rothstein, the reference is silent as to the function of GTRAP3-18 as a general regulator of cellular glycosylation. Indeed, Wahle is silent as to GTRAP3-18, as well as any interaction between GTRAP3-18 and GLAST1 transporter. As such, Wahle fails to remedy the deficiencies of Rothstein.

In summary, neither Rothstein nor Wahle disclose or suggest the role of GTRAP3-18 in modulating general cellular glycosylation. It is axiomatic that one cannot simply use the Applicants' disclosure as a "blueprint" to reconstruct, by hindsight, Applicants' claim. See *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985). As the cited references fail to teach or suggest, either implicitly or explicitly, each and every limitation of the present claims, the Office fails to establish a *prima facie* case of obviousness against the presently claimed invention. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

The Commissioner is hereby authorized to charge $65.00 as payment for the One-Month Extension of Time fee (small entity) to Deposit Account No. 07-1896. Additionally, the Commissioner is hereby authorized to charge any other fees that may be due in connection with the filing of this paper, or credit any overpayment to Deposit Account No. 07-1896, referencing the above-referenced Attorney docket number.

Respectfully submitted,

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